

2.3 HUMAN HEALTH HAZARD INFORMATION

Table 2-4 summarizes human health effects information obtained to date on chemicals used in lithographic blanket washes. Initial literature searches were limited to secondary sources such as EPA's Integrated Risk Information System (IRIS), the National Library of Medicine's Hazardous Substances Data Bank (HSDB), TOXLINE, TOXLIT, GENETOX, and the Registry of Toxic Effects of Chemical Substances (RTECS). The results of these literature searches are in the Administrative Record. These databases are established by other organizations as well as EPA, and are available by computerized online searching. They contain numeric and textual information that was used in developing the human health hazard summaries. These sources are considered secondary and no attempt has been made to verify the information contained in these sources. References typically are made to the database itself except for information taken from abstracts in TOXLINE and TOXLIT; in these cases, the author is cited with a notation to the database included in the text. Additionally, toxicologic data developed under the Office of Pollution Prevention and Toxics' Chemical Testing Program are incorporated in the human health hazard summary. Unpublished data submitted under TSCA §§ 8(d) and 8(e) are being reviewed and will be incorporated as appropriate in the final version of this document.

The "TOX ENDPOINT" column in Table 2-4 lists adverse toxicological effects that have been reported in the literature for animal or human studies. This is simply a qualitative listing of reported effects and does not imply anything about the severity of the effects nor the doses at which the effects occur. Furthermore, an entry in this column does not necessarily imply that EPA has reviewed the reported studies or that EPA concurs with the authors' conclusions. Toxicological effects are abbreviated as follows:

car = carcinogenicity

chron = chronic effects not otherwise listed. Target organ toxicity such as liver and kidney effects may be manifested by changes in size, structure, or function of the organ. For example, organ weight changes, changes in cell size or shape, or changes in enzyme activity associated with a particular organ are commonly reported endpoints in chronic toxicity studies.

dev = developmental toxicity, i.e., adverse effects on the developing embryo, fetus, or newborn

gene = genetic toxicity, such as point mutations or chromosomal aberrations

g.i. = gastrointestinal effects

hema = hematological effects, i.e., adverse effects on blood cells. Blood effects may involve changes in the number of blood cells as well as effects on their structure or function.

neuro = adverse neurological effects; includes a wide range of effects from serious neuropathology to transient CNS depression commonly seen with high exposures to solvents

repro = reproductive toxicity, i.e., adverse effects on the ability of either males or females to reproduce

resp = respiratory effects

LD₅₀ = the dose (usually from a single dosing or short-term exposure) lethal to 50% of a test population

The "RfD/RfC" is the EPA Reference Dose (RfD) or Reference Concentration (RfC). The RfD is an estimate of a daily exposure to the human population that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime. The RfD is usually expressed as an oral dose in mg/kg/day. The RfC is an analogous value for continuous inhalation exposure, usually expressed in mg/m³. The RfD/RfC values listed in Table 2-4 are used in the Hazard Quotient calculations shown in Section 3.4.

CHAPTER 2: DATA COLLECTION

The "NOAEL/LOAEL" is the no-observed-adverse-effect level or the lowest-observed-adverse-effect level, respectively. The NOAEL is an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects in the exposed population. The LOAEL is the lowest exposure level at which adverse effects have been shown to occur. The NOAEL/LOAEL values listed in Table 2-4 are used in the Margin of Exposure calculations shown in Section 3.4.

Table 2-4. Human Health Hazard Summary

Chemical Name	Ref No. [*]	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Alcohols, C ₁₂ -C ₁₅ , ethoxylated	33	68131-39-5	dermal				
			inhalation	neuro, g.i.			toxic effects based on acute or subacute (no. of doses not specified) oral study; the surfactant activity of this chemical will result in lung and eye irritation
Benzene, 1, 2, 4-trimethyl-	21	95-63-6	dermal			L - 5.71 mg/kg/day (urinary tract and enzyme effects) ^a	Included in TSCA Section 4 testing of C ₉ -hydrocarbons; 8(e) data available
			inhalation	neuro, chron ^b		L - 20 mg/m ³ (urinary tract and enzyme effects)	
Benzenesulfonic acid, dodecyl-	21	27176-87-0	dermal				
			inhalation				oral LD ₅₀ - 650 mg/kg ^c
Benzenesulfonic acid, dodecyl-, compounds with 2-aminoethanol	31	26836-07-7	dermal	g.i.		N - 5 mg/kg/day (dermal)	data from dodecylbenzenesulfonic acid, triethanolamine salt studies
			inhalation				
Benzenesulfonic acid, dodecyl- compounds with 2-propanamine	32	26264-05-1	dermal				SAT report ^k ; the surfactant activity of this chemical will result in lung irritation
			inhalation				
Benzenesulfonic acid, (tetrapropenyl)-, compounds with 2-propanamine	32	157966-96-6	dermal	neuro (amine salt)			SAT report; the surfactant activity of the chemical will result in lung irritation
			inhalation				
Benzenesulfonic acid, C ₁₀ -C ₁₆ -alkyl derivatives, compounds with 2-propanamine	32	68584-24-7	dermal	sensitizer			SAT report; the surfactant activity of the chemical will result in lung irritation
			inhalation				

Chemical Name	Ref No.	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Butyrolactone	21	96-48-0	dermal			L - 500 mg/kg/day ^d (fetotoxicity)	
			inhalation	dev, repro, resp		L - 500 mg/kg/day ^d (fetotoxicity)	toxic effects based on oral studies
Cumene	29	98-82-8	dermal	chron, g.i.	0.4 mg/kg/day (chron) ^d		toxic effects based on acute or subacute study (no. of doses not specified)
			inhalation	dev, repro, neuro, chron, resp	1.4 mg/m ³ (chron) ^d		TSCA §4, SIDS data available
Diethanolamine	17	111-42-2	dermal	repro, neuro, chron, g.i., hema		L - 32 mg/kg/day (chron, hema)	
			inhalation	repro, neuro, chron, hema		L - 14 mg/kg/day (chron, hema, decreased body weight gain) ^d	toxic effects based on oral studies; TSCA §4 review, SIDS dossier available
Diethylene glycol monobutyl ether	27 28	112-34-5	dermal	hema		N - 191 mg/kg/day	TSCA §4, SIDS reviews available
			inhalation	dev, repro, chron, hema		N - 14 ppm	no effects observed
Dimethyl adipate	4	627-93-0	dermal			L - 5.71 mg/kg/day (resp) ^a	TSCA §4 review available
			inhalation	resp		L - 20 mg/m ³ (resp)	toxic effects based on study using mixture of dibasic esters
Dimethyl glutarate	4	1119-40-0	dermal			L - 5.71 mg/kg/day (resp) ^a	TSCA §4 review available
			inhalation	resp		L - 20 mg/m ³ (resp)	toxic effects based on study using mixture of dibasic esters

Chemical Name	Ref No. [*]	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Dimethyl succinate	4	106-65-0	dermal			L - 5.71 mg/kg/day (resp) ^a	TSCA §4 review available
			inhalation	resp		L - 20 mg/m ³ (resp)	toxic effects based on study using mixture of dibasic esters
Dipropylene glycol monobutyl ether	21	29911-28-2	dermal	neuro			dermal LD ₅₀ - 5860 µL/kg ^c
			inhalation				oral LD ₅₀ - 1620 µg/kg ^c
Dipropylene glycol methyl ether	9 30	34590-94-8	dermal			N - (5 mL/kg) 4750 mg/kg/day	TSCA §4 dermal testing planned
			inhalation	neuro, chron, resp		L - (200 ppm) 1213 mg/m ³ (increased kidney weight) ^e	
Distillates (petroleum), hydrotreated middle	22	64742-46-7	dermal				equivocal skin tumor response in mice through dermal exposure, positive Ames assay in multiple strains, with and without activation. No increased frequency of micronuclei in mouse bone marrow cells
			inhalation				
Ethoxylated nonylphenol	13 25	9016-45-9 26027-38-3 68412-54-4	dermal	chron, resp, g.i.		N - 500 mg/kg/day (dev/repro)	possible endocrine disrupter
			inhalation	dev, chron		N- 30 mg/kg/day ^d	
Ethylenediaminetetraacetic acid, tetrasodium salt	32	64-02-8	dermal				SAT report - low to moderate concern; poor skin absorption
			inhalation				
Fatty acids, methyl esters ^l	32	68002-82-4 67762-38-3 61790-69-0	dermal				SAT report; the surfactant activity of this chemical will result in eye and lung irritation
			inhalation				
Hydrocarbons, terpene processing by-products	32	68956-56-9	dermal				SAT report - low concern
			inhalation				

Chemical Name	Ref No.*	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
α -Limonene	16	5989-27-5	dermal			N - 250 mg/kg/day (increased hepatocyte nuclei and cytomegaly in male mice) ^d	
			inhalation	dev, repro, neuro, chron, hema		N - 250 mg/kg/day (increased hepatocyte nuclei and cytomegaly in male mice) ^d	
Linalool	18	78-70-6	dermal			L - 500 mg/kg/day (increased liver weight) ^d	
			inhalation	neuro, chron		L - 500 mg/kg/day (increased liver weight) ^d	toxic effects based on oral study
Mineral Spirits (light hydrotreated)	7 20	64742-47-8	dermal				dermal LD ₅₀ >5000mg/kg (rabbits) ^e limited evidence for carcinogenicity (IARC); appearance of papillomas at 50 mg for 80 weeks, no control data
			inhalation				oral LD ₅₀ - 8532 mg/kg ^f
N-Methylpyrrolidone	1 10	872-50-4	dermal	dev, repro		N - 237 mg/kg/day (dev, repro)	TSCA §4 review available
			inhalation	chron, resp, hema		N - (10 ppm) 40.5 mg/m ^{3e} (chron)	
Naphtha (petroleum), hydrotreated heavy	32	64742-48-9	dermal				SAT report - low moderate concern
			inhalation	resp, neuro			SAT report - low moderate concern; lung irritation

Chemical Name	Ref No.*	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Nerol	22	106-25-2	dermal				SAT report; dermal LD ₅₀ > 5000 mg/kg ^c
			inhalation	dev			SAT report; oral LD ₅₀ - 4500 mg/kg ^c
Oxirane, methyl, polymer with oxirane, monodecyl ether	32	37251-67-5	dermal				SAT report
			inhalation				
2-Pinanol	32	473-54-1	dermal				SAT report
			inhalation				
Plinols	32	72402-00-7	dermal				no information available
			inhalation				no information available
Polyethoxylated isodecyloxypropylamine	32	68478-95-5	dermal				SAT report
			inhalation				
Poly(oxy-1,2-ethanediyl), α -hexyl- ω -hydroxy-	32	31726-34-8	dermal				SAT report
			inhalation				
Propanoic acid, 3-ethoxyethyl ester	22	763-69-9	dermal				dermal LD ₅₀ - 10000 mg/kg
			inhalation				oral LD ₅₀ - 5000 mg/kg ^c
Propylene glycol	11 21 29	57-55-6	dermal		20 mg/kg/day (hema) ^d		no evidence of carcinogenic effects by dermal exposure; questionably positive Salmonella test (host-mediated) with Strains G46 and TA1530; positive for chromosome aberrations in hamster fibroblasts, negative in other mammalian cells
			inhalation	chron, hema	20 mg/kg/day (hema)		toxic effects based on oral studies; no evidence of carcinogenic effects by oral exposure

Chemical Name	Ref No.*	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Propylene glycol monobutyl ether	6 15	5131-66-8	dermal			N - 11.40 mg/kg/day	no systemic effects at highest dose
			inhalation	chron, g.i.		N - 400 mg/kg/day ^{d,f}	toxic effects based on oral studies
Sodium bis(ethylhexyl) sulfosuccinate	12	577-11-7	dermal			N - 50 mg/kg/day ^d (repro/dev)	sensitizer
			inhalation	dev, neuro, g.i.		N - 50 mg/kg/day ^d (repro/dev)	toxic effects based on oral studies
Sodium hydroxide	32	1310-73-2	dermal	corrosive			
			inhalation	resp			
Sodium xylene sulfonate	32	1300-72-7	dermal				SAT report
			inhalation				
Solvent naphtha (petroleum), heavy aromatic	32	64742-94-5	dermal				SAT report - moderate concern
			inhalation				SAT report - moderate concern
Solvent naphtha (petroleum), light aliphatic	32	64742-89-8	dermal	hema		N - 370 mg/kg/day ^a (hema)	SAT report
			inhalation			1300 mg/m ³ (hema)	
Solvent naphtha (petroleum), light aromatic	26	64742-95-6	dermal			L - 140 mg/kg/day (repro, dev) ^{a,g}	
			inhalation	dev, repro		L - (100 ppm) 491 mg/m ³ (repro, dev) ^{a,g}	
Solvent naphtha (petroleum), medium aliphatic	5	64742-88-7	dermal	neuro, resp		L - 481 mg/kg/day (increased leucocytes) ^{a,h}	
			inhalation	neuro, chron, resp, hema		L - (294 ppm) 1683 mg/m ^{3e} (increased leucocytes) ^h	

Chemical Name	Ref No.*	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
Sorbitan, mono-9-octadecanoate	8	1338-43-8	dermal			N - 125 mg/kg/day (liver, kidney effects) ^d	
			inhalation	chron, g.i., hema		N - 125 mg/kg/day (liver, kidney effects) ^d	toxic effects based on oral studies
Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivatives	19	9005-64-5	dermal			N - 500 mg/kg/day (maternal tox/repro) ^d	
			inhalation	chron, g.i., hema		N - 500 mg/kg/day (maternal tox/repro)	toxic effects based upon oral studies
Sorbitan, monolaurate	32	5959-89-7	dermal				SAT report
			inhalation	chron, g.i., hema			
Sorbitan, tri-9-octadecanoate, poly(oxy-1,2-ethanediyl) derivatives	32	9005-70-3	dermal				SAT report
			inhalation	chron, g.i., hema			
Soybean oil, methyl ester	32	67784-80-9	dermal				SAT report
			inhalation				
Soybean oil, polymerized, oxidized	32	68152-81-8	dermal				SAT report
			inhalation				
Stoddard solvent	2	8052-41-3	dermal	chron, g.i., hema		L - 137 mg/kg/day (hema) ^{a,i}	
			inhalation	dev, neuro, chron, resp, g.i.		L - (84 ppm) 481 mg/m ³ (hema) ^{e,i}	
Tall oil, special	32	68937-81-5	dermal				SAT report
			inhalation				

Chemical Name	Ref No. ^a	CAS No.	Worker Exposure	Toxicity Endpoint	RfD/RfC	NOAEL (N) or LOAEL (L)	Comment
α-Terpineol	21	98-55-5	dermal				SAT report - low moderate concern
			inhalation				oral LD ₅₀ s - 5170 mg/kg (rats) and 1208 mg/kg (mice) (mice-RTECS Search, 1995)
Terpinolene	21	586-62-9	dermal				SAT report; oral LD ₅₀ - 4390 mg/kg (rats) ^c
			inhalation				
Tetrapotassium pyrophosphate	23	7320-34-5	dermal			N - 1250 mg/kg/day (chron) ^{d,j}	
			inhalation	chron		N - 1250 mg/kg/day (chron) ⁱ	toxic effects based on oral studies
Xylene	3 14 29	1330-20-7	dermal		2 mg/kg/day (neuro) ^d	L - 150 mg/kg/day (increased liver weight) ^d	TSCA §4 review available
			inhalation	dev, neuro, chron, resp	(2 mg/kg/day) 7 mg/m ³ (neuro) ^d	L - 50 mg/m ³ (dev)	RfD based on oral study

^a Dermal NOAEL/LOAEL or RfD based upon inhalation data

^b Chron - refers to chronic effect not otherwise listed; commonly includes target organ toxicity such as liver and kidney effects

^c Available LD50's given only for those chemicals for which no other toxicity information was found

^d Inhalation or dermal LOAEL/NOAEL or RfD based upon oral data

^e Original data given in ppm, converted to mg/m³ using the following conversion:

$$\text{mg/m}^3 = \frac{\text{ppm} \times \text{molecular weight (grams)}}{24.45}$$

^f NOAEL based upon subacute study

^g Molecular weight of 120 based upon C9 fraction

^h Molecular weight of 40 based upon average molecular weight of components

ⁱ Molecular weight of 140 based upon average molecular weight of components

^j For rats: ppm in diet x 0.05 = mg/kg/day

^k SAT reports are generated by the OPPT Structure-Activity Team to predict toxicity based on analog data and/or structure-activity considerations.

^l Fatty acids refers to: Fatty acids, C₁₆-C₁₈, methyl esters; Fatty acids, C₁₆-C₁₈ and C₁₈-unsatd., compounds with diethanolamine; and, Fatty acids, tall oil, compounds with diethanolamine

* The following references (with the exception of Nos. 24, 26, 27, 28, 29, and 32) were developed from online database searches conducted between February and May 1995. The toxicity data from these references are reported in Table 2-3 and in most cases the primary references were not reviewed.

1. Becci PJ, Knickerbocker MJ, Reagan EI, et al. 1982. Teratogenicity study of N-methylpyrrolidone after dermal application to Sprague-Dawley rats. *Fund Appl Toxicol* 2:73-76.
2. Carpenter CP, Kinkead ER, Geary DL, et al. 1975. Petroleum hydrocarbon toxicity studies. III. Animal and human responses to vapors of Stoddard solvent. *Toxicol Appl Pharmacol* 32:282-297.
3. Condie LW, et al. 1988. Oral toxicity studies with xylene isomers and mixed xylenes. *Drug Chem Toxicol* 11:329-354.
4. E.I. DuPont de Nemours and Company. 1985. FYI-OTS-0885-0433 INIT. Inhalation reproduction study in rats exposed to dibasic esters (DBE) (final Report) with attachments and cover letter dated 032792. Performed by Haskell Laboratory for Toxicology and Industrial Medicine. Washington DC: Office of Pollution Prevention and Toxics, U.S. EPA. EPA Doc. No. 88-920001533.
5. Exxon. 1980. TSCA sec 8(e) submission 8EHQ-1079-0312 follow up. A 12 Week Inhalation Toxicity Study of MRD-78-26 (Isopar C) in the Rat. Bio/dynamics Inc. Project No. 78-7092B. Washington, DC: Office of Toxic Substances, U.S. Environmental Protection Agency.
6. Hazleton. 1989. Hazleton Laboratories. 86-890000466S. A 91-day subchronic percutaneous toxicity with attachments, cover sheets and letter dated 061289 (sanitized). Office of Pollution Prevention and Toxics, U.S. EPA, Washington, D.C., 7pp.
7. IARC. 1989. International Agency for Research on Cancer. Occupational Exposures in Petroleum Refining. In: IARC Monographs on the Evaluation of Carcinogenic Risk to Humans, Vol. 45. Lyon, France: IARC.
8. Ingram AJ, et al. 1978. Short-term toxicity study of sorbitan monooleate (Span 80) in rats. *Food Cosmet Toxicol* 16(6):535.
9. Landy TD, Yano BL. 1984. Dipropylene glycol monomethyl ether: a 13-week inhalation toxicity study in rats and rabbits. *Fundam Appl Toxicol* 4:612-617.
10. Lee KP, Chromey NC, Culik R, et al. 1987. Toxicity of N-methyl-2-pyrrolidone (NMP): Teratogenic, subchronic, and two-year inhalation studies. *Fund Appl Toxicol* 9:222-225.
11. Litton Bionetics, Inc. 1974. Mutagenic Evaluation of Compound FDA 71-56, Propylene Glycol. Report No. LBI-2446-294, FDABF-GRAS-294. Kensington, MD: Bionetics, Inc. NTIS PB245450/2.
12. MacKenzie K, Henwood S, Foster G, et al. 1990. Three-generation reproduction study with dioctyl sodium sulfosuccinate in rats. *Fundam Appl Toxicol* 15(1):53-62.
13. Meyer O, Haubro Anderson P, Hansen EV, Larsen JC. 1988. Teratogenicity and *in vitro* mutagenicity studies on nonoxynol-9 and -30. *Pharmacol Toxicol* 62:235-238.
14. Mirkova E, et al. 1983. Prenatal toxicity of xylene. *J Hyg Epidem Microb Immun* 27337-343.

15. Notox. 1987. Toxicology Research and Consultancy C.V. 86-890001253. Assessment of the oral toxicity, including hemolytic activity, of Dowanol-PnB in the rat: 14-day study. Office of Pollution Prevention and Toxics., U.S. EPA, Washington, DC., 82 pp.
16. NTP. 1990. National Toxicology Program. Toxicology and Carcinogenesis Studies of d-Limonene (CAS No. 5989-27-5) in F344/N Rats and B6C3F1 Mice (gavage Studies). Research Triangle Park, NC: NTP. NTP TR 347.
17. NTP. 1992. National Toxicology Program. NTP Technical Report on Toxicology Studies of Diethanolamine (CAS no. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F₁ mice. Technical Report Series No. 20. U.S. Department of Health and Human Services.
18. Powers KA, Beasley VR. 1985. Toxicological aspects of linalool: a review. Vet Hum Toxicol 27:484-486.
19. Price CJ, George JD, Marr MC, et al. 1992. Final Report on the developmental toxicity of polyoxyethylene sorbitan monolaurate (CAS no. 9005-64-5) in Sprague-Dawley (CD:) rats on gestational days 6 through 15. NTIS Technical Report (NTIS/PB93-123800); 130pp.
20. RTECS. 1993. Registry of Toxic Effects of Chemical Substances. MEDLARS Online Information Retrieval System, National Library of Medicine.
21. RTECS. 1994. Registry of Toxic Effects of Chemical Substances. MEDLARS Online Information Retrieval System, National Library of Medicine.
22. RTECS. 1995. Registry of Toxic Effects of Chemical Substances. MEDLARS Online Information Retrieval System, National Library of Medicine.
23. Shimoji N, Matsushima Y, Imaida K, et al. 1988. Subchronic oral toxicity of potassium pyrophosphate prior to long term carcinogenic studies in F344 rats. Eisei Shikensho Hokoku 106:66-72.
24. SIDS Initial Assessment Profile.
25. Smyth HF, Jr., Calandra JC. 1969. Toxicologic studies of alkylphenol polyoxyethylene surfactants. Toxicol Appl Pharmacol 14:315-334.
26. U.S. EPA. 1991. U.S. Environmental Protection Agency. RM1 Report on C9 Aromatic Hydrocarbon Fraction. Office of Pollution Prevention and Toxics. Washington, DC.
27. TSCA §4 Study: 90-day dermal toxicity study.
28. Gingell R, et al. 1996. Toxicity of diethylene glycol butyl ether. Occupational Hygiene 2:293-302.
29. U.S. EPA. 1994. U.S. Environmental Protection Agency. Health Effects Assessment Summary Tables. Annual Update. Cincinnati, OH: Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, U.S. EPA.

30. U.S. EPA. Date not given. Chronic Skin Absorption of Propylene Glycol Methyl Ether (33B) and Dipropylene Glycol Methyl Ether (50B) in Rabbits. Washington, DC: Office of Toxic Substances, U.S. EPA. Doc #86-890001219.
31. Zondlo MM. 1993. Final report on the safety assessment of sodium dodecylbenzenesulfonate/TEA-dodecylbenzenesulfonate/sodium decylbenzenesulfonate. J Am Col Toxicol 12:279-309.
32. No information found in sources searched.
33. Bio/Dynamics, Inc. 1992. Initial Submission: Ethoxylated alcohol C12-15: Acute oral toxicity study in rats with cover letter dated 081092. TSCATS/431537. EPA/OTS Doc # 88-920006788.